VDH VIRGINIA DEPARTMENT OF HEALTH

Virginia Department of Health
Botulism: Guidance for Health Care Providers
Key Medical and Public Health Interventions after Identification of a Suspected Case

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1. Epidemiology

Botulism is a rare but serious illness caused by a nerve toxin produced by the gram-positive, anaerobic, spore-forming bacterium *Clostridium botulinum*. *Clostridia* bacteria that are capable of producing botulinum toxin are commonly found in soil, however, the toxin is only produced under conditions that promote spore germination, growth, and toxin production. Growth and toxin formation require an anerobic environment, moisture, neutral to alkaline pH, and an energy source (such as protein or sugar).

Botulinum toxins are the most potent biological toxins known. They inhibit acetylcholine release at the neuromuscular junction which leads to a descending flaccid paralysis that begins with cranial nerve palsies and typically progresses to extremity weakness and respiratory failure. In general, treatment involves supportive care, mechanical ventilation if needed, and rapid administration of botulinum antitoxin.

While botulinum neurotoxin is primarily produced by *C. botulinum*, strains of *Clostridium baratii*, *Clostridium butyricum,* and *Clostridium argentinense* produce botulinum toxin rarely. Seven types of neurotoxins (A–G) and hybrid or mosaic toxins (e.g., C/D, D/C, and A/F that were originally reported as type H) have been recognized. Human disease is caused primarily by toxin types A, B, E, and, rarely, F.

Botulism occurs worldwide and all persons are susceptible. Botulism is rare in the United States and Virginia. Approximately 100–200 cases of botulism are reported annually in the United States. Most reported cases of botulism (about 70%) are infant botulism. In the eastern United States, botulism is primarily caused by botulinum toxin type B, while toxin type A predominates in the western part and toxin type E predominates in Alaska. About three cases are reported annually in Virginia.

Clostridium botulinum toxin is designated as a Category A bioterrorism agent (i.e., it is easily disseminated or transmitted and is associated with a higher rate of mortality than a Category B agent). *Botulinum* neurotoxin-producing species of *Clostridium* are also designated as a select agent, which

means that they could be developed as bioterrorism agents and that possession, use or transfer of these organisms requires registration with CDC or USDA. If botulism is suspected or confirmed, the local health department (LHD) must be notified **immediately** so that a public health investigation can be initiated. To locate your local health department, see the VDH Local Health Department Locator.

Typically, botulism syndromes are categorized based on how the illness was acquired or its mode of transmission. Currently, there are six types of botulism: foodborne, infant, wound, adult intestinal toxemia (also known as adult intestinal colonization), iatrogenic, and inhalational. Infant, foodborne, and wound botulism are the most common, while adult intestinal toxemia, iatrogenic, and inhalational botulism are much less common. Each type is described below. Regardless of the mode of transmission, the clinical manifestations of botulism are essentially the same.

One case of botulism is considered a **medical emergency** because botulism can be fatal and rapid treatment is needed. **One case of foodborne botulism** is also considered a potential **public health emergency** because of the possibility that other people had the same food exposures.

Foodborne
Foodborne botulism occurs because of consumption of preformed botulinum toxin, most commonly with homemade foods that are improperly canned, preserved or fermented. Foods that are most commonly contaminated are home-canned vegetables, cured pork and ham, and smoked or raw fish. Commercially canned foods rarely cause botulism. Consuming certain kinds of homemade alcohol (e.g., prison wine also known as “pruno” or “hooch”) can also result in foodborne botulism. Foodborne botulism can be prevented by using sound home-preservation methods. See the USDA Complete Guide to Home Canning.

Infant
Infant botulism (i.e., intestinal botulism), the most common form of botulism, occurs with ingestion of *C. botulinum* spores that subsequently germinate in the intestine and produce toxin. Children under 12 months of age can be affected and most cases occur in those aged 6 weeks to 6 months.

Wound
Wound botulism occurs, rarely, when spores get into an open wound and reproduce in an anaerobic environment and produce toxin. Wound botulism has been reported among people who inject certain drugs (e.g., black tar heroin) and people with traumatic injuries.

Adult Intestinal Toxemia
Adult intestinal toxemia (also known as adult intestinal colonization) botulism is a very rare kind of botulism that occurs in immunocompromised adults, those using antimicrobials, or those with an anatomical or functional bowel abnormality, by the same mechanism as infant botulism.

Iatrogenic
Iatrogenic botulism occurs from accidental overdose of injectable botulinum toxin used for cosmetic or medical procedures. On occasion, public health agencies receive reports of iatrogenic botulism. For example, on March 7, 2023, the National International Health Regulations Focal Point for Germany alerted the World Health Organization (WHO) of five cases of iatrogenic botulism in health institutions in Turkey.

Inhalational
Inhalational botulism is a form of botulism that does not occur naturally. It is caused by aerosolizing botulinum toxin and has been reported in the laboratory setting. Aerosolization of toxins could potentially be used for a bioterrorism attack. Clinically, inhalational botulism cannot be differentiated from naturally occurring forms.

2. Clinical Manifestations

According to CDC, it should be noted that early clinical manifestations of botulism and the progression of neurologic signs and symptoms are sometimes misdiagnosed by treating clinicians. It is important to suspect the diagnosis as soon as possible because delayed administration of botulinum antitoxin (or immune globulin for infant botulism) can lead to a worse outcome. Other diagnoses that botulism has been misdiagnosed as include myasthenia gravis, Guillain-Barré Syndrome, stroke, Lambert-Eaton Syndrome, meningitis, encephalitis, tick paralysis, and psychiatric conditions.

In general, the most commonly reported symptoms among patients with botulism are dysphagia, blurred vision, slurred speech, difficulty speaking, hoarse voice, gastrointestinal symptoms, dry mouth, shortness of breath, and diplopia. The most common signs are descending paralysis, ptosis, and ophthalmoplegia. Fever and altered mental status are NOT typically seen in botulism.

Infant botulism is the most common type of botulism that is reported in the U.S., and foodborne botulism is the most common type globally. Infant botulism and adult intestinal toxemia botulism share a common pathophysiology. The intestine becomes colonized with *Clostridia* bacteria that are capable of producing botulinum toxin in situ, and illness results.

Botulism leads to a protracted flaccid paralysis that can last for weeks to months. Death that occurs during the acute stage of the illness is usually a result of respiratory failure. In the later stage of the illness, death is usually caused by complications of prolonged intensive care and hospitalization—this may include ventilator-associated pneumonia, other types of infections, or thromboembolic disease. Prompt administration of botulinum antitoxin reduces the extent and severity of paralysis. The benefits of this may be a patient who spends less time on a ventilator, in intensive care, or in the hospital.

Despite the information above, almost all patients with botulism can survive with supportive care alone even without botulinum antitoxin. In the early 1900s, case fatality rates (CFR) were about 70%; however, the current botulism CFR is about 5% due to improvements made in intensive care.

Foodborne Botulism
- **Incubation period:** Typically, 12–72 hours (range 2 hours–8 days)
- **Symptoms**: Early symptoms are often fatigue, weakness, and vertigo, followed by double and blurred vision, dry mouth, and difficulty swallowing and speaking as a result of toxin effects on the cranial nerves. Flaccid, symmetric, and descending paralysis is a typical symptom, developing from the shoulders to upper and lower arms, thighs, and calves. The paralysis can affect the muscles used for breathing. In severe cases, respiratory failure may occur. Gastrointestinal symptoms, including nausea, vomiting, constipation, abdominal swelling and less commonly, diarrhea, may occur. Loss of consciousness and fever typically do not occur, unless a complicating infection is also present.

Infant Botulism

- **Incubation period:** Unknown
- **Symptoms**: Early symptoms are often constipation, loss of appetite, weakness, lethargy, poor suck, ptosis, difficulty swallowing, altered cries, loss of head control, and hypotonia. Infant botulism has a wide spectrum of clinical severity, ranging from mild illness to sudden infant death. Progression is more severe in those aged less than two months.

Wound Botulism

- **Incubation period:** Approximately 7 days (range 4 days–14 days)
- **Symptoms**: Similar to foodborne botulism

Adult intestinal toxemia botulism

- **Incubation period:** Unknown
  Symptoms: Similar to foodborne botulism. The onset is generally gradual and less acute. In some cases, diarrhea due to *Clostridium difficile* co-infection has been reported.

Iatrogenic Botulism

- **Incubation period:** Days to weeks
- **Symptoms:** Generalized weakness, dysphagia, and respiratory distress are the primary symptoms of iatrogenic botulism resulting from overdose of botulinum toxin.

Inhalational Botulism

- **Incubation period:** Approximately 6–80 hours
- **Symptoms:** Mucus in throat, difficulty swallowing, dizziness, difficulty moving eyes, mild pupillary dilation and involuntary eye movement, indistinct speech, unsteady gait, and extreme weakness.
  Note: Inhalational botulism does not occur naturally; therefore, intentional aerosolization of botulinum toxin should be suspected if a cluster of cases occurs.

3. Laboratory Testing and Diagnosis

Notification when Botulism is Suspected

If botulism is suspected, the healthcare provider should immediately report the case to the local health department per Virginia's disease reporting regulations. The local health department will discuss options for public health testing. If VDH approves testing, specimens may be sent to the Division of Consolidated Laboratory Services (DCLS). VDH will facilitate notification and shipment to DCLS. Specimens potentially containing *C. botulinum* or botulinum toxin should **never** be shipped to DCLS without prior approval. The emergency on-call staff member for DCLS can be reached 24 hours a day/7 days per week at 804-335-4617.

Laboratory Biosafety

Botulinum toxins are extremely poisonous and exposure to the toxin is the primary laboratory hazard. Laboratory personnel **must** be alerted if botulism is suspected so they can take appropriate precautions. All laboratory work on specimens suspicious of containing toxin should be performed using standard precautions and biosafety level 2 (BSL-2) containment criteria. Additional containment and personnel precautions, such as those recommended for BSL-3, are recommended during activities with a high potential for aerosol or droplet precaution. To prevent the release of aerosols, laboratorians should use a class II biologic safety cabinet (BSC) when processing specimens. For additional information, refer to

the American Society for Microbiology's Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases: Botulinum Toxin (2013).

Diagnostic Testing and Sample Collection

Please note that treatment with botulinum antitoxin should be based on the clinical presentation and findings and should **not** be delayed by waiting for confirmatory test results. Because the prompt administration of antitoxin begins with diagnostic suspicion of botulism instead of diagnostic certainty (because confirmatory lab testing takes time), CDC recommends the following regarding the diagnosis of botulism:

- Consider botulism when myasthenia gravis or Guillain-Barré syndrome are suspected and in a patient with unexplained symmetric cranial nerve palsies, with or without paresis of other muscles
- Conduct thorough, serial neurologic examinations to detect the neurologic deficits of botulism and their progression
- If botulism is suspected, immediately contact the local or state health department's emergency on-call staff to arrange an emergency expert clinical consultation and, when indicated, request botulinum antitoxin from CDC

Confirmation of botulism relies on 1) detecting botulinum toxin in a clinical specimen (or food, if applicable), or 2) isolating *Clostridium botulinum* from a clinical specimen. Toxin testing is primarily performed using a mouse bioassay. While in-vivo mouse testing is routinely performed and considered the "gold standard" to confirm the presence of botulinum neurotoxin, other in-vitro tests are available for the detection and activity of botulinum toxin. These include immunoassays to detect botulinum toxin and cell-based assays to detect the biological activity of botulinum toxins. In the future, it's possible that these newer tests may take the place of in-vivo mouse testing.

As an example of diagnostic testing, in a case of suspected adult intestinal toxemia, multiple stool specimens would be sent to evaluate for the presence of botulinum toxin and viable *Clostridia* bacteria that are capable of producing botulinum toxin (viable neurotoxigenic *Clostridia*). Serum specimens looking for botulinum toxin should also be sent. If foodborne botulism is suspected, food specimens should be evaluated for botulinum toxin.

In botulism, routine laboratory tests such as complete blood counts (CBCs), examination of cerebrospinal fluid (CSF) by lumbar puncture, and imaging studies are typically normal. These studies may be helpful to rule out other possible diagnoses such as a stroke or Guillain-Barré Syndrome (in which elevated CSF protein concentrations are frequently seen).

When evaluating causes of weakness, electrodiagnostic studies such as electromyograms (EMGs), repetitive nerve stimulation (RNS) testing, and nerve conduction studies (NCSs) may help identify the cause. Distinctive classical findings of botulism include: an increment in the compound motor nerve action potential amplitude, with RNS rates of 30–50 Hz; fibrillation; decreased recruitment of muscle units; decreased duration of muscle unit potentials with EMG; and decreased motor-evoked amplitude on an NCS with otherwise normal findings. However, early in the course of botulism, electrodiagnostic testing may be normal. CDC recommends using electrodiagnostic testing to assist in diagnosis of a suspected botulism case, when feasible. In a botulism outbreak setting, electrodiagnostic testing may not be needed because suspicion of the illness may be based on clinical findings alone. For further

discussion of electrodiagnostic studies in botulism, see CDC's Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021.

One of the most important aspects of evaluating a patient with generalized weakness is asking about known risk factors for botulism. Risk factors for wound botulism may include injection drug use, whereas eating home-canned food may raise suspicion of foodborne botulism. According to CDC, clinicians should ask patients about possible exposures to well-described sources of botulinum toxin, while keeping in mind that absence of such exposures does not exclude the possibility of botulism.

Because of the dangers of manipulating botulinum toxin, botulism testing is conducted at a Laboratory Response Network (LRN) laboratory, such as DCLS. Sentinel laboratories package and ship specimens to DCLS for testing. In some cases, additional testing at CDC might be performed.

Table 1 lists recommended specimens for botulism testing and instructions for handling and shipping. Whenever possible, clinical specimens should be collected before treatment with antitoxin. For questions about specimen collection, the DCLS emergency on-call staff member can be reached 24 hours a day/7 days a week at 804-335-4617.

Case Definitions used by Public Health

The current CDC case definitions for botulism are from 2011 and available at https://ndc.services.cdc.gov/case-definitions/botulism-2011/. Note that a case definition is set of uniform criteria used to define a disease for public health surveillance. Case definitions enable public health to classify and count cases consistently across reporting jurisdictions and they should not be used by healthcare providers to determine how to meet an individual patient's healthcare needs.

Table 1. Sample collection for suspected botulism cases and testing at DCLS*†

Laboratory Test and Turnaround Time	Samples†	Amount	Instructions
Botulism laboratory confirmation (mouse bioassay) Estimated turnaround time: 4 business days upon specimen receipt; 8 business days upon testing of stool enrichment cultures (if applicable)	Stool	10–50 grams	Place into sterile unbreakable container (do not use transport media). Store specimens at 4°C. Ship on cold packs as soon as possible.
	Enema	20 mL	If an enema is performed because of constipation, use a minimal amount of fluid (preferably sterile, nonbacteriostatic water) to obtain the specimen and prevent diluting the toxin unnecessarily. Place in a sterile unbreakable container. Store specimens at 4°C. Ship on cold packs as soon as possible.
	Serum	10 mL sera (~20 mL whole blood)	Use red top or serum separator tubes (SST) to obtain serum (no anticoagulant) before administration of antitoxin. Red top tubes should be spun down and serum should then be placed in a sterile tube before sending to DCLS. SST tubes should be spun down and the entire tube should be sent to DCLS. Store specimens at 4°C. Ship on cold packs as soon as possible. For infant cases, DCLS will accept 1–2mL of serum to perform limited testing if appropriate volume cannot be collected. Note: Serum volumes <5 mL will provide presumptive results and collection of additional serum might be required; whole blood should not be sent as it typically undergoes excessive hemolysis during transit.
	Gastric aspirate or vomitus	20 mL	Place in sterile unbreakable container. Store specimens at 4°C. Ship on cold packs as soon as possible.
	Tissue, exudate, or wound swab	Small amount of tissue / 2 swabs	Place specimen(s) into sterile unbreakable container(s) with anaerobic transport media. Store and transport without refrigeration.
	Food samples‡	100–150 grams or as available in original container	Food should be left in their original containers if possible. If transferring, place food into a sterile unbreakable, puncture resistant container and label carefully. Place containers individually in leak-proof containers (e.g., sealed plastic bags) to prevent cross-contamination during shipment. Store specimens at 4°C. Ship on cold packs as soon as possible. Note: Empty containers with remnants of suspected foods can be examined.

*Adapted from American Society for Microbiology's Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases: Botulinum Toxin (2013). If botulism is suspected, notify the local health department immediately to discuss the case and laboratory testing. If VDH approves testing, specimens may be sent to Division of Consolidated Laboratory Services (DCLS) with the DCLS Test Request Form. Include the name of the test on the form. For questions about collecting specimens or for notifying DCLS when submitting specimens, contact the DCLS Emergency Officer available 24/7 at 804-335-4617.

†Acceptable samples by form of botulism: Foodborne: stool/enema, serum, vomitus, gastric aspirate, and food. Wound: serum, debrided tissue, swab from wounds, and stool (if foodborne botulism is also suspected). Infant: stool/enema, rectal swab, serum, and potential sources. Adult intestinal toxemia: stool/enema and serum.

‡Food collection should be coordinated through the LHD and the VDH Division of Surveillance and Investigation Foodborne Epidemiology team; food samples should be collected under chain of custody using the DCLS Chain of Custody Form

4. Treatment

The diagnosis and treatment of botulism should be made on the basis of the patient's history, clinical presentation, and clinical findings. **Treatment should be initiated once botulism is clinically diagnosed (or highly suspected) and should not wait for laboratory confirmation. Botulinum antitoxin should be administered as soon as possible (within 48 hours of symptom onset and ideally within 24 hours).** The antitoxin does not reverse paralysis but stops its progression and can prevent respiratory compromise in certain patients. Confirmatory laboratory testing for botulism may be negative even when the patient truly has the illness; this emphasizes the importance of administering botulinum antitoxin presumptively when clinical suspicion is high.

For non-infant botulism cases, botulism antitoxin heptavalent (brand name BAT) is available only at CDC. BAT is an equine-derived preparation of antibodies that bind and neutralize botulinum toxins A through G. Botulinum antitoxin must be specific to the type of botulinum toxin that is affecting the patient. Therefore, BAT contains a mixture of immune globulin fragments against the seven botulinum neurotoxins noted above. BAT is indicated for the treatment of children and adults with symptomatic botulism. To obtain BAT, the patient's physician should consult with the local health department and CDC (available 24/7 at 770-488-7100). Patients with suspected botulism should be treated with BAT regardless of underlying medical conditions, or age, sex, or other demographic characteristics. Pregnancy is not considered a contraindication to administration of botulinum antitoxin.

Regarding the administration of botulinum antitoxin later in the course of illness, CDC recommends the following:

- Patients with suspected botulism whose symptoms or signs (e.g., paralysis) are progressing should be treated with BAT regardless of the time that has elapsed since symptom onset
- Patients with suspected botulism whose symptoms and signs are not progressing and who have no remaining voluntary muscle function are less likely to benefit from antitoxin treatment, especially if >7 days have passed since symptom onset, because toxin is infrequently detected beyond this point of illness

For infant botulism cases, human-derived botulism antitoxin (known as BabyBIG® or BIG-IV (Botulism Immune Globulin Intravenous—Human) is available only through the California Department of Public Health's Infant Botulism Treatment and Prevention Program (www.infantbotulism.org). To obtain BabyBIG®, the patient's physician should contact the on-call physician of the Infant Botulism Treatment and Prevention Program at 510-231-7600 (available 24/7) to review the indications for such treatment. Note that in a bioterrorism attack, BabyBIG® should not be administered.

BabyBIG is indicated for the treatment of infant botulism caused by toxin types A or B in a patient less than one year of age. BabyBIG only contains human-origin anti-A and anti-B botulinum antitoxins. Infant botulism syndrome that is caused by other botulinum toxin types (or thought to be caused by other toxin types) can be treated with the equine-derived heptavalent botulism antitoxin (BAT).

In addition to antitoxin, meticulous supportive care (e.g., artificial ventilation and nutritional support) should be provided when indicated. No other specific treatments have been shown to be effective for botulism, including activated charcoal, polyethylene glycol, cholinergic agonists, plasmapheresis, or antimicrobials. Certain medications should be used with caution in patients with botulism, as they may

pose a risk: antimicrobials including clindamycin, aminoglycosides, and penicillins (risks and benefits should be weighed in the use of these for comorbid conditions), magnesium, calcium, monoamine oxidase inhibitors, and neuromuscular blocking agents. Further detail can be found in CDC's Clinical Guidelines for Diagnosis and Treatment of Botulism, 2021.

5. Postexposure Prophylaxis

Antitoxins are not useful for postexposure prophylaxis against botulism. Asymptomatic people with exposures to botulism toxins or *Clostridium botulinum* spores should be monitored closely for signs and symptoms and should be treated promptly with antitoxin at the first signs of illness.

6. Vaccination

Currently, there is no licensed vaccine for commercial use.

7. Infection Control

Person-to-person transmission of botulinum neurotoxin or botulism does not occur. Standard Precautions are adequate for the care of patients with botulism. Patients do not need to be isolated. Botulinum toxin cannot be absorbed through intact skin but can be absorbed through nonintact skin and mucous membranes. According to the medical literature, no case of person-to-person botulism has been described, including in patient care settings. Despite this, people exposed to body fluids and/or stool from a patient with botulism should be informed about the early symptoms of the illness and advised to seek care if these symptoms develop.

Infants with botulism can shed *C. botulinum* and toxin in the stool for weeks to months after onset. Hand hygiene among caregivers is critical. Diapers should be disposed of so that other people or animals cannot come into contact with them. People with open cuts or wounds on their hands should wear gloves when handling soiled diapers. Close contact with other infants (e.g., sharing crib and toys) should be avoided while excretion might be continuing.

Foods suspected of contamination should be promptly removed from potential consumers and submitted to public health for testing. Those known to have eaten contaminated food should be kept under close medical observation for symptoms and/or signs of botulism. If these develop, patients should be promptly treated with botulinum antitoxin and followed closely in a medical setting.

8. Decontamination

If exposure to the botulism toxin via aerosol inhalation is suspected, the clothing of those who are exposed must be removed and stored in labeled double plastic bags until it can be washed thoroughly with soap and water. The exposed persons must shower thoroughly with soap and water. Contaminated objects or surfaces should be cleaned with a 0.1% hypochlorite bleach solution to inactivate the botulism toxin.

9. Postmortem Practices

Appropriate precautions should be used for postmortem practices. This includes using a surgical scrub suit, surgical cap, impervious gown or apron with full sleeve coverage, eye protection (e.g., goggles or face shield), shoe covers, and double surgical gloves with an interposed layer of cut-proof synthetic mesh. Autopsy personnel should wear N-95 respirators during autopsies. Powered air-purifying respirators (PAPRs) equipped with high-efficiency particulate air (HEPA) filters should be considered for postmortem practices. Bodies infected with biological terrorism agents including *Clostridium botulinum* should not be embalmed.

10. Public Health Measures

- Suspected or confirmed botulism cases should be reported immediately to the local health department. See https://www.vdh.virginia.gov/health-department-locator/
- Laboratory specimens should be sent to DCLS for confirmation of agent and other studies after consultation and approval by VDH. For questions about specimen collection, the DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.
- Designated public health authority should begin an epidemiologic investigation. The activities include:
    - Collect detailed information from the patient and close contacts about the source of the exposure, in particular food history
    - Investigate contacts of the patient for compatible illness to identify a potential common exposure. Persons who may have consumed any contaminated food items should be monitored closely.
    - Suspected food items (e.g., home-canned foods) should be collected for possible testing. VDH's Office of Epidemiology will work with the U.S. Food and Drug Administration if commercially prepared food is implicated.
    - Implement control measures to prevent disease and additional exposures. For laboratorians or others potentially exposed who might have worked with the agent before identification as *Clostridium botulinum*, post-exposure monitoring might be recommended based on a risk assessment.

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